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Assistant General Counsel



January 22, 1999

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Docket Management Branch (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane  
Room 1061  
Rockville, Maryland 20852

RE: The Second Meeting of the Pharmacy Compounding Advisory Committee  
*64 Federal Register 886 (January 6, 1999)*

Dear Sir/Madam:

At the first meeting of the Pharmacy Compounding Advisory Committee, several issues were of concern to PhRMA members. In response to those concerns, we are submitting the enclosed comments and suggestions for the second meeting. Some of these may be relevant to the work of the Committee during its next meeting.

Several observers and Committee members noted that the Committee discussions were re-directed whenever a Committee member attempted to raise a scientific question. The work of the Committee, especially when it is considering whether specific substances should be included on the list of substances that may be used to compound medicines, must be grounded in sound science. That can only occur if the Committee members are allowed to discuss scientific issues. PhRMA urges FDA and the Committee to ground any decisions about substances suitable for compounding on sound science,

Several of the Committee members seemed to be unaware of, or not have any detailed knowledge of, FDA's existing adverse event reporting requirements for approved drug products. This system is central to FDA's ability to monitor drugs, once approved. Because of the importance of FDA's ability to monitor the use of all prescription drugs, PhRMA believes that the Advisory Committee needs to consider how FDA can monitor adverse events that may be associated with the use of compounded medicines. The Advisory Committee's consideration of safety concerns with compounded medicines, and the substances that might be used to compound medicines, would be enhanced by a clear understanding of the system that FDA uses to monitor the safety of FDA-approved drugs. Therefore, PhRMA recommends that FDA provide the Committee with a detailed briefing about the purpose and operation of the existing adverse event reporting system.

Because compounded drugs may also be associated with adverse events, FDA should be able to monitor such events, and to distinguish them from adverse events associated with the use of approved products. Therefore, PhRMA recommends that FDA

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modify its current system for reporting of such adverse events to incorporate information about adverse events that may be associated with compounded medicines.

FDA's requirements for chemistry and manufacturing controls, particularly as they relate to the quality, purity, and strength of ingredients and approved medicines, and the relevant ICH guidelines, are central to the safe manufacture of approved drugs. As the Committee considers the safe compounding of medicines from substances that are not ingredients in approved drugs and are not subject to a USP monograph, the Committee needs to consider ways that the compounding pharmacist can determine whether the ingredients used, as well as the compounded medicine, are of known and measurable quality, purity and strength. Public Citizen Health Research Group, in their comments to the Committee, urged FDA to require that compounded products contain a boxed warning stating that the product was not produced in a facility that meets good manufacturing practice guidelines. While PhRMA has no position on Public Citizen's labeling recommendation, PhRMA recommends that, to serve as a point of reference, FDA provide a detailed briefing to the Committee about FDA's requirements for chemistry and manufacturing controls for approved drugs.

The Committee discussed the use of a Certificate of Analysis as one method for pharmacists to determine that ingredients they purchase to compound medicines meet acceptable standards of quality, purity and strength. Yet some of the FDA Compounding Advisory Committee members seemed to have limited information about what constitutes a Certificate of Analysis, and how that information compares with the information manufacturers must have about substances they use as ingredients in approved medicines. Therefore, PhRMA recommends that FDA provide a detailed briefing to the FDA Advisory Committee about what constitutes a Certificate of Analysis and a comparison with the information FDA requires manufacturers of approved drugs to have for their ingredients.

Because compounded products will not have all of the information that normally accompanies an FDA-approved product, such as the name of the manufacturer and the expiration date, patients should be told that they are receiving a compounded product. Indeed, in their comments to the FDA Compounding Advisory Committee, Public Citizen urges FDA to require compounded products to contain a boxed warning that the drug has not been approved by the FDA. As an alternative to the boxed warning, perhaps FDA should require, either directly or through the memorandum of understanding with state boards of pharmacy, that the pharmacy include on the container in which the product is dispensed a label statement indicating that the medicine was compounded at that pharmacy.

FDA has distributed to Advisory Committee members written materials on many topics. However, in light of the complexity of many of the issues, Committee members may

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learn more from an oral presentation of key aspects of some FDA requirements for manufactured drugs, with an opportunity for questions.

We would be pleased to provide further information or answer any questions on any of these issues.

Sincerely,

A handwritten signature in cursive script that reads "Marjorie E. Powell". The signature is written in black ink and is positioned to the right of the word "Sincerely,".

Marjorie E. Powell

cc: Igor Cerny/CDER